Mundschenk et al. (WO 97/43407) merely represents Applicant's own prior teaching of the preparation and use of preferred inactivated bioactive peptides. It should be noted that the "bioactive" peptides described therein include a variety of toxins, and similar peptides, and hence are quite *unlikely* to be delivered to the body at all, or in any form, let alone directly to a surface within the mouth. Clearly nothing in the reference itself teaches or suggests buccal delivery in this manner, let alone using the formulation presently described and claimed.

Nor has the Examiner yet cited any reference that suggests the delivery of an "inactivated bioactive peptide" in the buccal cavity, using any system or approach whatsoever. In fact, Heiber et al. 5,766,620 is merely cited for the mere proposition that "peptides are buccally administratable". The Action ignores the fact, however, that Heiber et al. do not describe the peptides of the present invention, nor do the compositions of Heiber et al. include the use of benzalkonium chloride, particularly in the manner presently claimed.

Nor do Dondeti et al. or Siegel et al. remedy the defects of the previous two references, including those described above.

At its closest, Dondeti et al. merely describes the use of benzalkonium chloride as a *preservative*, and then only *in addition to* the use of 2-phenylethanol as an additional preservative. The effect of both preservatives, in turn, was evaluated *not* to determine their effect (collectively) on delivery, *per se*, but instead in view of the possible effects of such preservatives on "globule size" and on "ciliary beat frequency". These effects, however, are clearly unique to the "microcrystalline cellulose" composition of Dondeti et al., as compared to the present formulation, and to nasal, as compared to buccal, delivery.

Similarly, Siegel et al. investigate the effect of surfactants, including benzalkonium chloride, on the permeability of canine mucosa, using a variety of test molecules. At its *closest*, the reference evaluates the effect of benzalkonium chloride (at concentrations of 0.025%, 0.1% and 1.0%).on the permeability of insulin. Note that only the *lowest* of these concentrations is even within the most preferred enhancer concentration ranges of the present invention (see, page 6, lines 22-27 of the specification). The data at Table I of Siegel et al., however, shows that this concentration fails to provide *any* significant improvement as compared to the control. It is only at significantly higher concentrations (at or well exceeding Applicant's outermost concentration range) that "permeability" is increased. Rather than true permeability, however, the increase at these concentrations would presumably be due, in large part, to the severe disruptive effect the surfactant would be expected to have on membranes.

The rejection of claims 5 and 51 under Section 103(a) is respectfully traversed. Mundshenk, Dondeti et al. and Siegel et al. are distinguished for the reasons set forth above, and for others as well.

The only additional reference, namely Kamiya et al., is merely included as teaching the use of spraying to administer peptides. Putting aside its own deficiencies, this reference adds nothing to remedy the various shortcomings described above with respect to the combination of Mundshenk and either Dondeti et al. or Siegel et al. as set forth above.

Accordingly, reconsideration of the pending rejection and allowance of the claims as amended above is respectfully requested.

Respectfully submitted,

Dated: 08Nov2001

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